

## Complete Summary

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### GUIDELINE TITLE

Prevention of venous thrombosis.

### BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Prevention of venous thrombosis. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2006 May 3 [Various].

### GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Finnish Medical Society Duodecim. Prevention of venous thrombosis. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2006 Mar 17 [Various].

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## SCOPE

### DISEASE/CONDITION(S)

Venous thrombosis

### GUIDELINE CATEGORY

Prevention  
 Risk Assessment

### CLINICAL SPECIALTY

Family Practice  
Internal Medicine  
Neurology  
Obstetrics and Gynecology  
Surgery

## INTENDED USERS

Health Care Providers  
Physicians

## GUIDELINE OBJECTIVE(S)

Evidence-Based Medicine Guidelines collect, summarize, and update the core clinical knowledge essential in general practice. The guidelines also describe the scientific evidence underlying the given recommendations.

## TARGET POPULATION

Patients at risk for venous thrombosis

## INTERVENTIONS AND PRACTICES CONSIDERED

Risk Assessment

Classify patients into low, moderate, high risk groups

Prevention

1. Avoid immobilization before and after surgery
2. Avoid general anaesthetics
3. Optimize fluid balance
4. Start preventive therapy
5. Compression dressings or antiembolism stockings
6. Warfarin
7. Low molecular weight heparin (enoxaparin, dalteparin)
8. Aspirin
9. Fondaparinux, danaparoid, lepidurin
10. Protamine as an antidote to postoperative and post-traumatic bleeding

## MAJOR OUTCOMES CONSIDERED

- Efficacy of prophylactic measures at reducing the risk and rates of deep venous thrombosis and/or pulmonary embolism
- Side effects of therapy

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)  
Hand-searches of Published Literature (Secondary Sources)  
Searches of Electronic Databases

#### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence reviewed was collected from the Cochrane database of systematic reviews and the Database of Abstracts of Reviews of Effectiveness (DARE). In addition, the Cochrane Library and medical journals were searched specifically for original publications.

#### NUMBER OF SOURCE DOCUMENTS

Not stated

#### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

#### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

- A. Strong research-based evidence. Multiple relevant, high-quality scientific studies with homogenic results.
- B. Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.
- C. Limited research-based evidence. At least one adequate scientific study.
- D. No research-based evidence. Expert panel evaluation of other information.

#### METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses  
Systematic Review

#### DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

#### RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

#### COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

#### METHOD OF GUIDELINE VALIDATION

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

The levels of evidence [A-D] supporting the recommendations are defined at the end of the "Major Recommendations" field.

See the National Guideline Clearinghouse (NGC) summary of the American College of Chest Physicians guideline [Prevention of Venous Thrombosis](#)

#### Basic Rules

- Venous thrombosis is a common and dangerous disease that can, however, be treated and often prevented.
- Venous thrombosis of a bedridden patient can be asymptomatic--the first symptom may be pulmonary embolism.
- Early mobilisation, antiembolism stockings, low molecular weight heparin (LMWH), and warfarin are used for primary prevention. Aspirin (ASA) is primarily used for the prevention of arterial occlusion.
- Aspirin may also reduce the incidence of venous thrombosis ("Collaborative overview," 1994) [A] However, as evidence of benefit is lacking, aspirin is not anymore recommended as prophylaxis on e.g., long haul flights (Geerts, 2004)
  - On long flights it is recommended that high risk patients wear antiembolism stockings.
  - LMWH may also be used if the patient has known thrombophilia or a history of thromboembolism and is not on warfarin (one dose of prophylaxis half an hour prior to flight).
- If the patient is under 40 years of age and has a venous thrombosis without any causative factors, consider the possibility of a hereditary coagulation disorder.
- In addition to hereditary (intrinsic) factors there are extrinsic factors and conditions that contribute to venous thrombosis:
  - Previous venous thrombosis
  - Oral contraceptives
  - Pregnancy, labour, and puerperium 6 weeks
  - Surgery and tissue trauma
  - Varicose veins
  - Obesity
  - Polycythaemia, essential thrombocytosis, dehydration
  - Heart insufficiency and immobilisation
  - Paralysis, inactivity
  - Malignant diseases
  - Immobilization (cast, long flights)

## Prevention of Venous Thrombosis in Surgery

- Low risk (risk of venous thrombosis 2-3%)
  - Minor surgery (<30 min), no risk factors
  - Age <40, no risk factors
- Moderate risk (risk of venous thrombosis 10-30%)
  - Minor surgery, risk factors
  - Nonmajor surgery, no risk factors, age 40-60
  - Major surgery, age under 40, no risk factors
- High risk (risk of venous thrombosis 50-80%)
  - Major surgery, age >40 years, and earlier deep venous thrombosis or pulmonary embolism or cancer
  - Thrombophilia
  - Knee or hip arthroplasty, hip fracture
  - Major trauma, injury of the spinal cord
- The estimated risk of venous thrombosis in the above-mentioned risk groups is about 10%, 30%, and 60%, respectively. In classifying patients into risk groups, take into account both the personal predisposing factors and the type of surgery. Give prophylactic medication against thrombosis to patients belonging to the moderate or high-risk groups. Low-molecular-weight heparin (LMWH) is safe and easily administered at home. It should be used more often for the low-risk patients and the course of medication should be prolonged in high-risk patients.
- Immobilization increases the risk of thrombosis (e.g., an ankle fracture in a cast involves a 20% risk, and a fractured tibia in a cast a 60% risk).

## How to Prevent Thrombosis in Surgical Patients

- Avoid immobilization before and after surgery, avoid general anaesthetics and prefer spinal or epidural anaesthetics, optimize the fluid balance.
- Start preventive therapy before the operation, if possible (Hull et al., 1999) [C].
- Among the available physical measures the most common and easiest are compression dressings or a surgical stocking (Amaragiri & Lees, 2000; Wells, Lensing, & Hirsh, 1994; Agu, Hamilton, & Baker, 1999) [A], which in low-risk patients suffice as the only methods of prevention. Their usefulness has been shown in surgical and obstetric patients.
- Early mobilization does not mean that the patient is placed in a sitting position: mere sitting may even increase the risk of thrombosis.
- Warfarin can also be used for prophylaxis, as it is practical and inexpensive, and can be used when long-term prophylaxis is needed (e.g., a fractured pelvis and long immobilization). The use of warfarin involves the risk of bleeding and requires regular monitoring.
- Heparin is effective in reducing the incidence of deep vein thrombosis (Handoll et al., 2002; Palmer et al., 1997; Howard & Aaron, 1998) [A]. LMWHs have displaced ordinary heparin because of their higher efficacy and easy administration (once daily). If the immobilization is prolonged, continue heparin treatment until the patient is able to get up again. The most common treatment period is 1-2 weeks. Prophylactic treatment with LMWH is safe and often possible to carry out at home. Treatment duration is 4 weeks in hip (Hull et al., 2001) [A] and knee prosthesis surgery and in cancer surgery (Bergqvist et al., 2002) [B], 6 weeks during pregnancy and puerperium. In a

high-risk group the treatment can be continued with warfarin for 6-12 weeks. A nurse making home visits may help in the administration of LMWH.

- The usual prophylactic treatment scheme with LMWH
  - Moderate risk patients
    - Enoxaparin 20 (to 40) mg subcutaneous (s.c.) 2 hours before surgery and then the same amount once daily
    - Dalteparin 2500 IU 2 hours before surgery and then the same amount once daily
  - High risk patients
    - Fondaparinux 2.5 mg s.c. once daily, started 6 h after surgery. Fondaparinux is an inhibitor of coagulation factor X, that prevents venous thrombosis in association with orthopaedic surgery more efficiently than enoxaparin (Turpie, et al., 2004; Agnelli et al., 2005; Garces & Mamdani, 2002; "Fondaparinux," 2001) [A].
    - Enoxaparin 40 mg s.c. 12 hours before surgery and then the same amount once daily
    - Dalteparin 5000 IU 12 hours before surgery and then the same amount once daily
- Adverse effects: postoperative and post-traumatic bleeding. The antidote is protamine.

### Prevention of Venous Thrombosis in Internal Medicine and in Neurological Diseases

#### Risk Factors for Venous Thrombosis

- Heart failure and other non-surgical high-risk patients
- Heart failure and myocardial infarction
- Pulmonary embolism is a common cause of death of patients with infarction of the brain. The risk can be lowered with early mobilisation, antiembolism stockings, and LMWH. Haemorrhage complications diminish the benefits.
- Cancer
- Severe infection

#### How to Prevent Thrombosis in Medical Patients

- LMW heparin has replaced ordinary heparin. LMWH therapy should be considered for all patients who are at bed rest for more than 3 days and who have one or more of the above-mentioned risk factors. The efficacy of this prophylactic treatment has not been documented as well as in surgical patients.

### Prevention of Venous Thrombosis During Pregnancy

- Carried out in special care units

#### High Risk of Thromboembolism

- A venous thrombus above the knee, or pulmonary embolism during an earlier pregnancy.

- Patients with a hereditary or acquired blood coagulation disorder and a previous venous thrombosis. (In antithrombin III deficiency the risk is so high that prophylactic treatment must always be given, even if the patient has no history of thrombosis).
  - Acquired coagulation disorders include (e.g., lupus anticoagulant and myeloproliferative diseases [e.g., polycythaemia vera, essential thrombocytosis]).

#### Treatment in Special Care Units

- Start prophylactic treatment with LMWH after confirming the pregnancy, or at the latest on weeks 16-18. Mini-heparin treatment is not sufficient! Continue antithrombotic therapy for 6 weeks after parturition; however, at the time of delivery the drug can be changed to oral warfarin, which is contraindicated during pregnancy. The risk of thrombosis is highest at the end of the pregnancy, and higher doses of LMWH are often used.
- The initiation of heparin treatment depends on the risk: in women who have had thromboembolism during an earlier pregnancy or on oral contraceptives the treatment should always be started on week 24 at the latest.
- Prophylactic treatment in patients with activated protein C (APC) resistance due to genetic defect of factor V (see EMB guideline on "Thrombophilia [inherited]"):
  - Heterozygotes who have not had a thrombosis: prophylactic treatment is recommended only in cases of caesarean section or immobilization.
  - Heterozygotes who have had a thrombosis: prophylactic treatment is recommended during pregnancy and puerperium.
  - Homozygotes: prophylactic treatment is recommended regardless of whether the patient has had a thrombosis or not.

#### Thrombocytopenia and Thrombosis as Complications of Heparin Treatment

- Early thrombocytopenia is benign and caused by aggregation of thrombocytes.
- Severe immunologically mediated thrombocytopenia leads to activation of thrombocytes and endothelial damage, causing arterial thrombi.
- Symptoms are caused by arterial or venous thrombosis during weeks 1-3 of the treatment. Classical days for the condition to emerge are the fifth and the tenth day from the beginning of the treatment.
- The laboratory finding is a clear decrease in the thrombocyte count (or a value below 100 in one measurement). Thrombocytopenia occurs in approximately 1% of LMWH users (Prandoni, et al., 2005)
- In the follow-up of heparin treatment, haemoglobin and thrombocyte values should be taken at 1-week intervals for 4 weeks.
  - Actions are required if the thrombocyte count falls below 50% from the baseline value, if the thrombocytopenia is progressing, or if the antithrombotic treatment proves ineffective.
  - Do not start warfarin treatment before the thrombocyte count is normalized.
- Platelet transfusions are contraindicated. Consult a haematologist.
- Alternative anticoagulants: fondaparinux, danaparoid, lepidurin

### Related Evidence

- Pneumatic compression has lower incidence of thromboembolism than aspirin, warfarin, or low molecular weight heparins after knee arthroplasty. A combination of regimes might be best strategy to incorporate their advantages (Westrich et al., 2000) [B].

### Definitions:

#### Levels of Evidence

- A. Strong research-based evidence. Multiple relevant, high-quality scientific studies with homogenic results.
- B. Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.
- C. Limited research-based evidence. At least one adequate scientific study.
- D. No research-based evidence. Expert panel evaluation of other information.

#### CLINICAL ALGORITHM(S)

None provided

### EVIDENCE SUPPORTING THE RECOMMENDATIONS

#### REFERENCES SUPPORTING THE RECOMMENDATIONS

[References open in a new window](#)

#### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Concise summaries of scientific evidence attached to the individual guidelines are the unique feature of the Evidence-Based Medicine Guidelines. The evidence summaries allow the clinician to judge how well-founded the treatment recommendations are. The type of supporting evidence is identified and graded for select recommendations (see the "Major Recommendations" field).

### BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

#### POTENTIAL BENEFITS

Accurate risk assessment and prevention of venous thrombosis

#### POTENTIAL HARMS

- The use of warfarin involves the risk of bleeding and requires regular monitoring.
- Low-molecular-weight heparin (LMWH) can cause postoperative and post-traumatic bleeding.
- Thrombocytopenia and thrombosis are complications of heparin.

- Severe immunologically mediated thrombocytopenia leads to activation of thrombocytes and endothelial damage, causing arterial thrombi. This complication occurs more often with ordinary heparin than with low-molecular-weight heparin.

## CONTRAINDICATIONS

### CONTRAINDICATIONS

- Oral warfarin is contraindicated during pregnancy.
- Platelet transfusions are contraindicated for treatment of thrombocytopenia and thrombosis as complications of heparin treatment.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Staying Healthy

### IOM DOMAIN

Effectiveness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Prevention of venous thrombosis. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2006 May 3 [Various].

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2004 Mar 6 (revised 2006 May 3)

### GUIDELINE DEVELOPER(S)

Finnish Medical Society Duodecim - Professional Association

#### SOURCE(S) OF FUNDING

Finnish Medical Society Duodecim

#### GUIDELINE COMMITTEE

Editorial Team of EBM Guidelines

#### COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Author: Markku Ellonen

#### FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

#### GUIDELINE STATUS

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This guideline updates a previous version: Finnish Medical Society Duodecim. Prevention of venous thrombosis. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2006 Mar 17 [Various].

#### GUIDELINE AVAILABILITY

This guideline is included in a CD-ROM titled "EBM Guidelines. Evidence-Based Medicine" available from Duodecim Medical Publications, Ltd, PO Box 713, 00101 Helsinki, Finland; e-mail: [info@ebm-guidelines.com](mailto:info@ebm-guidelines.com); Web site: [www.ebm-guidelines.com](http://www.ebm-guidelines.com).

#### AVAILABILITY OF COMPANION DOCUMENTS

None available

#### PATIENT RESOURCES

None available

#### NGC STATUS

This NGC summary was completed by ECRI on August 30, 2005. This NGC summary was updated by ECRI on July 13, 2006.

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